

UNTREATED SYPHILIS IN THE MALE NEGRO

BACKGROUND AND CURRENT STATUS OF PATIENTS IN THE TUSKEGEE STUDY

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THIS report is one of a series¹⁻⁹ concerning a study of untreated acquired syphilis in the male Negro in Macon County, Alabama, conducted by the Venereal Disease Program, Division of Special Health Services, United States Public Health Service. Previous reports have dealt with: the various abnormalities found in untreated syphilitic individuals and nonsyphilitic controls at the time of the initial examination; the life expectancy of the respective groups after twelve years' observation; the abnormalities among untreated syphilis patients with special attention to the cardiovascular system after six years' observation; and a comparison of physiologic changes in the groups after sixteen years' observation.

HISTORICAL BACKGROUND

The natural history of untreated syphilis, that is, the incidence and types of complications, the occurrence of latency, and the incidence of spontaneous cure in the host, unaided by specific therapy, has been surmised chiefly from the work and reports of Boeck and Bruusgaard in Oslo, Norway. In 1927, Bruusgaard,¹⁰ and, more recently, Gjestland,¹¹ have sought out and re-examined the survivors of the original members of Boeck's syphilis clinic in which, from

This article is one of a series on untreated syphilis in the male Negro which the Venereal Disease Program, Division of Special Health Services, plans to assemble into a monograph. Single copies of the monograph will be made available upon request to the Venereal Disease Program, Division of Special Health Services, U. S. Public Health Service, Washington 25, D. C.

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1889 to 1910, mercury, the only drug available, was withheld from the patients as being of questionable value and, perhaps, of harm. This had constituted the only well-studied and documented group of untreated syphilis patients in medical literature.

In 1946, Rosahn¹² published results of a retrospective study of untreated syphilis cases coming to autopsy at Yale University hospitals.

As described in detail by Olansky and associates,⁶ the present study arose as an outgrowth of one of the earliest extensive blood-testing and syphilis treatment programs in the United States, sponsored by the Rosenwald Fund and then by the Public Health Service in Macon County, Alabama, in 1930 and 1932, respectively. These surveys revealed a shocking incidence of syphilis which marked the area to be one of "saturation" with the untreated disease. After treatment of the acute cases, a group of Negro men over 25 years of age, who volunteered for the examination, were selected for study. It was agreed that they would be kept under observation by the local health officer and public health nurse; that they would be examined at intervals, to check on their physical status; and they would not be given specific therapy for syphilis, if syphilitic. A group of approximately 400 individuals was selected, in all of whom the diagnosis of syphilis was made in accordance with criteria laid down at the time and detailed elsewhere.¹ A control group, selected to match with respect to age and general social level, was taken from among the nonsyphilitic population examined in the survey, and was considered as nonsyphilitic on the basis of seronegativity and freedom of history or signs of the disease. At the time the groups were selected from a farming community of poor, rural, southern Negroes, the socioeconomic and health status was generally so low that the only difference between syphilitic and control groups was in the presence or absence of evidence of syphilis.

In the fall of 1951, a fourth survey of the survivors of the original study group was begun. An effort was made to locate as many of the men as possible in order to gather maximum clinical and serologic information, as well as to determine whether or not the advent of the "antibiotic era" had defeated the project as a study of untreated syphilitic men. It was anticipated that history taking would be more important, and perhaps more difficult, than previously, in respect to type, amount, date, and source of any treatment received. A special field investigator was assigned to the survey. He helped the nurse follow-up worker in locating and transporting the patients and, also, sought information relating to treatment and socioeconomic status from each patient.

The beginning of this survey coincided with a visit to the United States of Gjestland of Norway, the chief worker in the current re-examination and re-evaluation of the survivors of the Boeck-Bruusgaard study. At the invitation of the Division of Venereal Disease, he visited Tuskegee and observed the first group of patients as they were examined. He saw, first hand, the remarkable socioeconomic and racial difference between the rural Alabama Negro farmers and the fair-skinned Norwegians whom he has been studying.

As the first aged men trooped into the hospital for examination, Dr. Gjestland and the examiners felt as if they were witnessing a strange and historic

procession. Their feelings were similar to those of Bruusgaard who wrote in 1929, "It produced a curious impression to see these patients after so many years . . . several of them over 70 . . . a strikingly large percent of the cases were free of clinical symptoms . . . many of these patients had apparently tried to undermine their health by an unreasonable mode of life, but had not succeeded."

Despite the similarities, however, certain striking differences between these two studies of untreated syphilis are apparent and are listed in Table I.

TABLE I. TABULAR LISTING OF DIFFERENCES IN THE UNTREATED SYPHILIS STUDIES IN ALABAMA AND IN NORWAY

	ALABAMA	NORWAY
Study population composition	Rural Negro men	White men and women
Control	Nonsyphilitic controls observed	No controls
Percentage autopsied of those who have died	63.3 per cent	24.3 per cent
Patient motivation for study participation	Volunteers with social incentives	Sickness and disability
Treatment status	Small amounts, especially in younger men	Less treatment available, especially in early years of study
Clinical facilities	Newer x-ray, EKG, and serologic techniques	Best medical facilities of the time (1925-1927)
Spinal fluid examination	Most of the syphilitic patients had spinal fluid examinations at start of study	No routine spinal fluid examination reported
Selection of patient material	Acute syphilis and younger patients treated and omitted at start of study; early and late latent patients studied and followed	Only early, untreated syphilis included

METHODS

Many of the techniques used in this survey were based on previous experience, for example, timing. The "slack" season, between fall harvest and spring planting, has been most advantageous for the periodic examinations. The modern Veterans Administration Hospital in Tuskegee was utilized. An experienced public health nurse and follow-up worker contacted the men by letter and home visits.⁹ Transportation to and from the hospital was provided. Incentives in the form of free, hot lunches and free medicine (for diseases other than syphilis) were given. One of the chief innovations in the current survey was emphasis on epidemiologic methods of tracing and contacting every possible survivor of the original study group. With the assistance of a trained field investigator, and with the cooperation of Venereal Disease Control officers in distant cities and states, most of the individuals now included in the study group have been traced; 209 of the total group (syphilitic patients and controls) are known to be dead, 332 are known to be living, and 59 are considered lost from observation, although efforts still are being made to trace them. Nine men still living in Macon County did not cooperate during the recent examination. These

men, too, are being observed, although "at a distance"; news of their illness or disability is readily available. A few examinations were made during home visits to farmers who were isolated or apathetic. In several instances, the patient was surprised during his morning plowing and asked to step in the shade of the nearest tree for an on-the-spot history, physical examination, and blood-letting. The survey team, consisting of a physician, nurse, and an interviewer-investigator, worked in Macon County from November, 1951, to June, 1952. Table II shows the number of examinations performed in this recent survey.

TABLE II. DISTRIBUTION OF SYPHILITIC AND NONSYPHILITIC PATIENTS EXAMINED IN THE 1951-1952 SURVEY

	NONSYPHILITIC PATIENTS	SYPHILITIC PATIENTS	TOTAL
Examined in Macon County, Alabama	93	139	232
Examined outside of Macon County	12	21	33
Total examined	105	160	265

THE STUDY POPULATION

During twenty years of observation, the study population has undergone changes, most significant of which are due to higher mortality rates among the syphilitic individuals. Before such changes can be properly evaluated, the composition of the study group from the beginning of the study should be reviewed. During 1932-1933, 412 syphilitic and 204 nonsyphilitic Negro men were selected for study. During 1938, at the time of the second physical examination, 14 untreated syphilitic individuals were added to the group. Reports on this study population, published during the course of the study, have included varying numbers of syphilitic and nonsyphilitic patients. This has been due to different interpretations by the various clinicians and analysts in regard to the criteria set up for the selection of study patients.

Prior to the preparation of reports based on the results of the 1951-1952 survey of the patients, a complete review of the records was undertaken to determine, as nearly as possible, which patients actually met the study criteria as originally set up and had maintained their original status during the twenty years of observation, 1932 to 1952. Questionable case histories were discussed by two clinicians, a serologist, and a record analyst, all of whom are closely associated with the study. It was determined, as a result of this careful consideration, that six individuals (four in the syphilitic and two in the control group) did not meet the criteria set up for inclusion in the study. These, in addition to the 14 persons who were added to the syphilitic group in 1938 and who, therefore, were under observation for only 14 years, are presently excluded from the syphilitic group. Also excluded are 10 individuals in the original nonsyphilitic group who acquired syphilitic infection at some time during the 1932 to 1952 period of observation.

With these exclusions, the current series of reports is based on the case histories of 408 syphilitic and 192 nonsyphilitic individuals. Of the 408 syphilitic patients, 208 were living, 41 are of unknown status, and 159* were known to be dead at the beginning of the 1951-1952 survey. Of the nonsyphilitic group, 124 were living, 18 were of unknown status, and 50* were known to be dead.

The exclusion of the 18 syphilitic patients and 12 control patients from this series of reports does not mean that care and examination of these latter patients will be discontinued. An attempt will be made, as in the case of the other study patients, to follow these individuals through to autopsy, where findings at that time may prove to be as informative as those for the major study group.

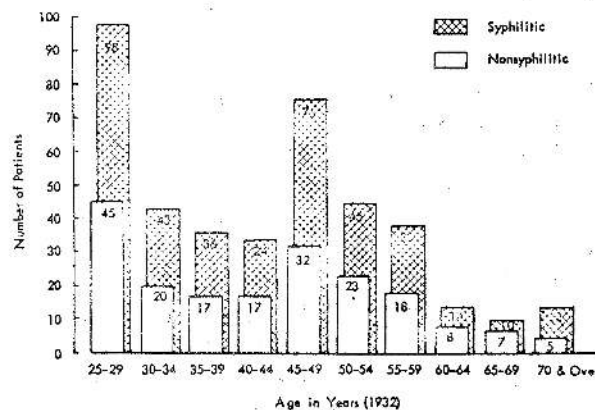


Fig. 1.—Distribution of study population by age in 1932, showing the ratio of syphilitic to nonsyphilitic patients.

AGES

Age grouping is one of the chief classifications used in this and previous reports. Most abnormalities are noted with respect to age group, syphilitic patients being compared to nonsyphilitic controls. The importance of comparable numbers in each age group was recognized at the start of the study.

Shortly after the syphilitic individuals were selected, nonsyphilitic subjects were sought to match them in age distribution according to a fixed ratio. Fig. 1 shows approximately twice as many syphilitic as nonsyphilitic subjects in each age group. The variations from this 2:1 ratio are not due to errors in the selection of the men in 1932, but rather to inconsistent ages given by certain individuals who were uncertain of their age.

*Six syphilitic patients and one nonsyphilitic patient died during 1952 after having been examined in the 1951-1952 survey. Since physical findings on these individuals have been included among those of the examined group, these patients are, for purposes of this report, considered to be living and examined. In the report on comparative life expectancies⁸ of the syphilitic and nonsyphilitic groups, these seven patients have been included among the deaths since the expectancies were based on mortality experience through the year 1952.

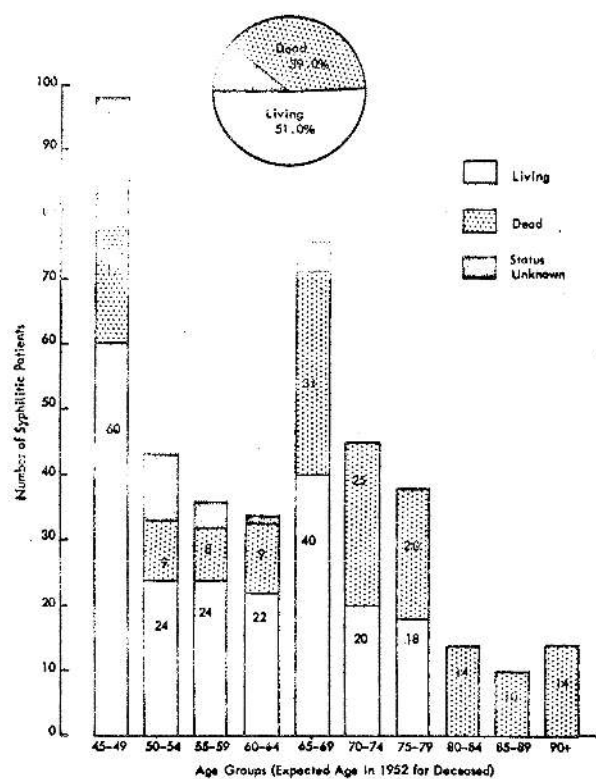


Fig. 2A.—Status of syphilitic patients in study population in 1952, considered as a whole and by age groups.

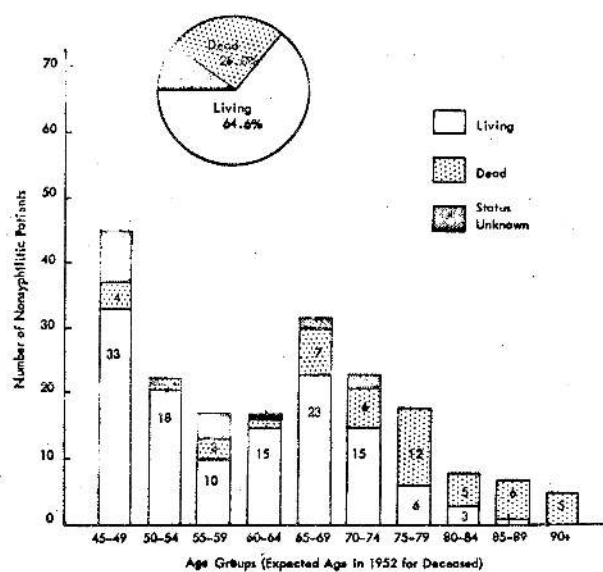


Fig. 2B.—Status of nonsyphilitic patients in study population in 1952, considered as a whole and by age groups.

STATUS OF THE STUDY POPULATION AFTER TWENTY YEARS

In Figs. 2A and 2B, the syphilitic and nonsyphilitic groups are compared after twenty years of observation. The majority of men lost or lapsed from observation are in the younger age groups; the young being traditionally more mobile than older, settled men. It is fortunate for the study, however, that many of the men who have moved out of Macon County continue to communicate with the public health nurse in Tuskegee or later return to their homesteads. The percentage of men lost from observation is comparable in each group, 10 per cent of the syphilitic patients and 9.4 per cent of the nonsyphilitic subjects. These figures add validity to the findings in the study, not only because they show that relatively few men have been lost from observation, but also because they indicate that interest in the diseased men has not overshadowed the follow-up study of the equally important nonsyphilitic controls.

MORTALITY COMPARED

The relative mortality of syphilitic patients compared to nonsyphilitic controls is shown somewhat differently in Figs. 2A, 2B, and 3. As all previous workers in this study have found, the most striking single feature distinguishing the syphilitic group from the nonsyphilitic is that the death rate is higher among the syphilitic men. Exactly how and why more of the syphilitic group has died is not clearly discernible, but the penalty which the syphilitic patients have paid in terms of life expectancy is well documented.⁵

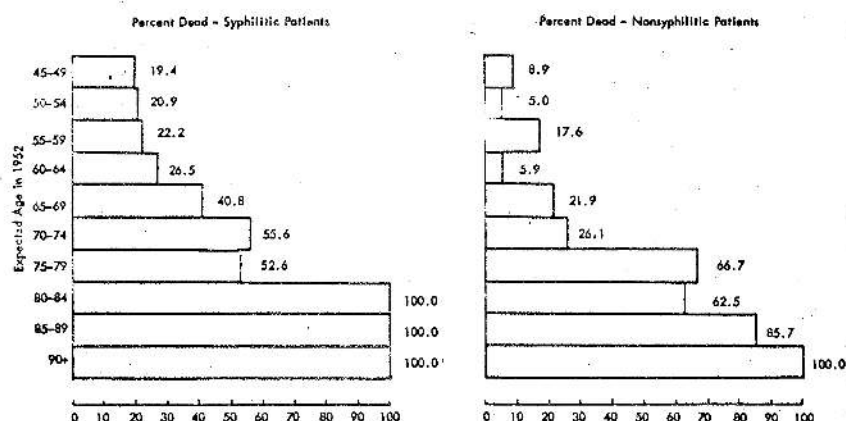


Fig. 3.—Mortality of syphilitic and nonsyphilitic patients, compared by percentage of each age group who have died during study period.

In Fig. 3, the mortality percentages of the deceased, by age group, are compared. Here again is seen the higher mortality of the syphilitic patients in each age group, with the exception of the 75- to 79-year-old category, where the death rate for nonsyphilitic is higher than that for syphilitic men. Such a difference serves to point out how the diseases of the aged enter the picture and seem to level the differences in the mortality experience of the men as they enter their later decades.

THERAPY RECEIVED BY SYPHILITIC PATIENTS INTERVIEWED IN 1952

It was expected that medical histories of the men in the study would reveal that they had received large amounts of antibiotic therapy for nonsyphilitic as well as syphilitic conditions. Questions were asked specifically as to time, source, duration, and amount of antibiotics received. Most of the men steadfastly denied receiving any antibiotic. As the same interviewing techniques were applied to nonsyphilitic as well as to syphilitic subjects, it was reassuring to discover that the antibiotic treatment rates of the two groups, according to historical data, were comparable: 27.5 per cent of the syphilitic patients examined in 1952 had received penicillin in varying amounts as compared to 32.6 per cent of the nonsyphilitic patients examined. The explanations for this low rate of exposure to antibiotics in this antibiotic era of medicine apparently are:

1. The economic plight of these men, who generally lack the means to afford medical care.
2. The relative well-being and hardiness of this aging but sturdy group of farmers.
3. The stoicism of these men as a group; they still regard hospitals and medicines with suspicion and prefer an occasional dose of time-honored herbs or tonics to modern drugs.

Many of the men have never been examined by any physician other than the Public Health Service officer who comes to Tuskegee periodically for surveys. Even these physicians had to overcome the apathy of the men at first, until they became accustomed to the examinations.

It is the practice of Public Health Service officers to refer men who develop syphilitic or nonsyphilitic conditions requiring therapy to the proper sources of treatment. Nevertheless, a few of the men have, on their own, sought and received antisyphilitic treatment in varying amounts. Some were treated by private physicians, a few had been inadvertently rounded up and sent to rapid treatment centers by health department workers who were unaware of the research project. Some of the patients were given therapy because of positive serologic tests for syphilis (STS) or because of a history of infection; some even were treated for unrelated symptoms, rather than for specific complications of syphilis.

In Table III, a comparison is made of 8 subjects who received antisyphilitic treatment: of disease duration in relation to treatment, serologic tests, and age. These 8 men were selected from the total of 12 syphilitic patients who have a history of adequate treatment. Their histories exemplify some of the problems encountered in this study. Patient 225 was the first man in our group to receive penicillin, which was given to him for a nonsyphilitic condition (pneumonia); after fourteen years of inadequately treated syphilis, his STS became negative following adequate treatment. Patient 097, 71 years of age, was seroresistant after adequate treatment, which is not difficult to explain since he had already lived with his untreated syphilis for forty-seven years and had submitted to therapy only because it was advised "as a premarital precaution."

The arsenical treatment listed is small, and, according to quantitative standards agreed upon for the Sing Sing study,¹³ less than 12 injection units can be regarded as "no treatment" (an injection unit is one injection of arsenical or two of bismuth). When the years of untreated syphilis are calculated for each man by subtracting the date of lesion from the date of treatment, and the total of the differences considered, we find 133 years of untreated syphilis and 107 years of inadequately treated syphilis compared to 20 years of adequately treated disease. Note that these sums are obtained from analysis of histories of 8 of the men who had been treated, and who, at first glance, would have been dropped from a study of untreated syphilis.

TABLE III. MEDICAL HISTORY OF LESIONS AND THERAPY OF EIGHT SYPHILITIC PATIENTS WHO WERE EXAMINED IN 1952; SHOWING DURATION OF DISEASE BEFORE TREATMENT WAS RECEIVED

PATIENT CHART NUMBER	HISTORY OF LESION (DATE)	ARSENICAL		DATE OF ADEQUATE PENICILLIN TREATMENT	DISEASE DURATION IN YEARS			KAHN REACTION		AGE IN 1952
		NUM- BER	DATE		UN- TREATED	INADEQUATE TREATMENT	ADEQUATE TREATMENT	PRIOR TO TREATMENT	AFTER TREATMENT	
137	1924	5	1934	1951	10	17	1	negative	negative	45
188	1928	7	1931	1949	6	15	3	doubtful	doubtful	45
225	1933	8	1934	1947*	1	13	5	positive	negative	55
534	1922	8	1934	1949	12	15	3	doubtful	doubtful	52
540	1928	5	1934	1949	6	15	3	doubtful	negative	53
034	1915	6	1935	1951	20	16	1	positive	positive	62
239	1913	8	1934	1950	21	16	2	doubtful	negative	68
097	1903	0	—	1950†	47	0	2	positive	positive	71
Total years					133	107	20	3 of 8 became seronegative		
Average years					15.4	13.4	2.5			

*Penicillin received for 2 weeks continuously, for pneumonia.

†Therapy given to 71-year-old man as a premarital precaution.

In Fig. 4, the treatment status of 160 syphilitic men, who furnished reliable treatment histories, is analyzed according to the amount and adequacy of therapy, on the basis of the categories recommended by the workers in the Sing Sing study.* The surviving syphilitic group is now 70 per cent untreated, 22.5 per cent inadequately treated, and 7.5 per cent adequately treated; this is compared to 100 per cent untreated in 1932 when the study was begun.

In Table IV, therapy status in 1952 is designated by age groups.

*The Sing Sing criteria for "no treatment" is no treatment, or treatment of less than three months' duration with arsenicals and bismuth, or less than 12 injection units of arsenicals and/or bismuth. "Inadequate treatment" is treatment for three to ten months, or 12 injection units or more, but less than "adequate" treatment, or less than 2,400,000 units of penicillin. "Adequate treatment" is 20 injections each of arsenicals and bismuth, or 30 injection units within two years, or any completed rapid treatment schedule consisting of 2,400,000 units or more of penicillin.¹³

TABLE IV. THERAPY STATUS IN 1952 OF 160 SYPHILITIC PATIENTS WHO WERE EXAMINED

AGE IN 1952	NUMBER OF PATIENTS	UNTREATED	ARSENICALS		PENICILLIN	
			3 TO 11	12 TO 22	INTER-MITTENT	CONTINUOUS
45 to 49	39	4	22	1	9	3
50 to 54	19	3	9	1	2	4
55 to 59	22	7	11	1	2	1
60 to 64	20	7	6	0	5	2
65 to 69	27	13	5	1	7	1
70 to 74	15	10	1	0	3	1
75 and over	18	13	1	0	4	0
Total	160	57	55	4	32	12
Per cent	100.0	35.6	34.4	2.5	20.0	7.5

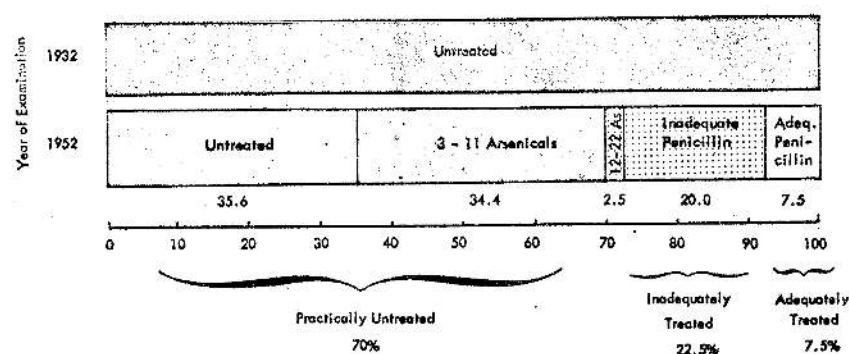


Fig. 4.—Specific therapy (classified according to Sing Sing study criteria, as described in text) received by syphilitic patients who were examined in 1952, as compared to untreated status of patients in 1932.

Fig. 5 compares age groups among the syphilitic men in terms of average man-years of untreated disease for each group. As, in Table V, the date of lesion is subtracted from date of therapy to obtain the number of years of untreated disease, so the number of such years for a given age group is divided by the number of individuals in that group to give an average. The average man-years of untreated disease are then plotted as a bar graph. The average syphilitic patient in the youngest age group (45 to 49 years of age) has had untreated disease for only 25.4 years, compared to the average man in the oldest age group (75 years of age and older) who has survived 49.6 years of untreated syphilis. Thus, modern treatment has altered this untreated syphilis study and made the task of analysis more complex. The task, as we see it, is not to discard all patients who have received any treatment, but rather to record as specifically as possible each date of injection and amount of therapy received. It does not seem warranted to underestimate the importance of following these syphilis

survivors indefinitely, since even in 1952 they are veterans of an aggregate of 5,494.5 man-years of untreated disease, in comparison to only 28.5 man-years of adequately treated disease.

TABLE V. DURATION OF SYPHILITIC DISEASE BY AGE GROUPS IN 1952; 160 PATIENTS

AGE IN 1952	NUMBER OF PATIENTS	MAN-YEARS OF DISEASE			AVERAGE MAN-YEARS BY TREATMENT STATUS		
		UNTREATED	INADEQUATE TREATMENT	ADEQUATE TREATMENT	UNTREATED	INADEQUATE TREATMENT	ADEQUATE TREATMENT
45 to 49	39	989	19.5	4.5	25.4	0.5	0.1
50 to 54	19	487	21	12	25.6	1.1	0.6
55 to 59	22	711	18	5	32.3	0.8	0.2
60 to 64	20	706	9	2	35.3	0.4	0.1
65 to 69	27	1,032.5	30.5	3	39.4	1.1	0.1
70 to 74	15	646	6	2	43.1	0.4	0.1
75 and over	18	893	18	0	49.6	1.0	—

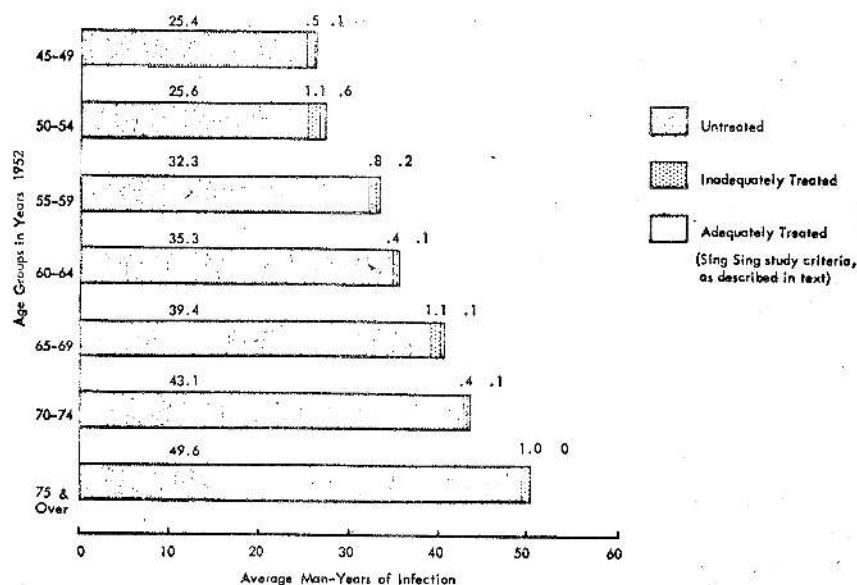


Fig. 5.—Average man-years of syphilitic infection among those examined in 1952, by treatment status and age groups.

Since the man-years of adequately treated disease represent such a small part of the total years of observation, and in most patients the treatment was administered many years after the date of the original infection, it is felt that the antibiotic era has not defeated the purpose of the study. Essentially, the study continues to be concerned with the effects of untreated syphilis, and on this basis, in certain of the papers in this series, the original syphilitic group is treated as an entity, regardless of the kind or amount of treatment.

MEDICAL HISTORY

Each patient was interviewed by both the physician and the interviewer-investigator. The chief complaint in each case was recorded. Most of the younger men had no complaints other than an occasional half-humorous reference to decreasing libido. Among the older men, complaints of backache and rheumatism were most frequent, even in several patients where clinical evidence of heart enlargement would suggest that cardiac symptoms could be expected. An attempt was made to estimate whether the individual seemed to be stoically inclined or hypochondriacal. As a whole, these men may be characterized as being almost as resigned to the infirmities of the flesh as they are to the vagaries of weather conditions which influence their crops; and they complain somewhat more vociferously about the latter. As in the past, the physician asked pertinent questions to elicit any cardiac symptoms, such as dyspnea, orthopnea, and angina. In an attempt to obtain as much specific information as possible, the interviewer would persist in questioning until he received answers such as this one from a 69-year-old farmer: "Well, with my old mule, I can plow all morning without resting, but with my young mule, it's a lot different." In this farmer's case, the pertinent fact is that he was plowing day after day with *any* mule! Crude as such interviewing techniques may seem, we were striving to evaluate cardiovascular syphilis in these men in terms of disability and distress, as well as in terms of mortality.

PHYSICAL EXAMINATIONS

All of the Alabama men were brought to the modern Veterans Administration Hospital in Tuskegee and were examined by a Public Health Service physician. Whenever diagnostic questions arose, consultation with specialists in ophthalmology, neurology, and cardiology was readily available and often utilized. As in past surveys, it was felt that a single clinical observer had the advantage of seeing the patient as a whole; this advantage might be lost if the patients were seen by a series of specialists who would be unknown to, and possibly mistrusted by, the patients. Examinations were limited to three or four a day to facilitate thoroughness.

Physical examination included the review of systems, blood pressure determinations from both arms, funduscopic examinations, and neurologic examination. As in previous surveys, the heart was examined with great care. For the first time in the study, stethographic records were obtained on each patient, the heart sounds were amplified and recorded synchronously with electrocardiograms and carotid artery pulse curves.* With stethographic records, the timing of suspicious murmurs was facilitated, and the recordings were a constant stimulus to the clinician to perform his best work so that the machine might not discover a murmur which he had missed. One factor of importance was the positioning of the patient. The best stethographic records could be obtained from the aged men only when they lay supine and relaxed on the couch. Nevertheless,

*We wish to acknowledge the skill and advice furnished at the beginning of the survey by Dr. Henry Eisenberg (Surgeon, U. S. Public Health Service) who instructed our technician, Mr. William C. Bowie, of the Veterans Administration Hospital, in obtaining the best possible stethographic records.

and indeed the larger part of such a program, yield little in the way of scientific credit for those having the vision, perspective, and ability to plan and work so well. Under these circumstances it is probably necessary for such ventures to be undertaken cooperatively, as was this one, with the early workers being given an opportunity to engage in other activities having prospect of earlier fruition.

Continuing close association of persons locally trusted and liked by the study group is essential to the success of a project.

A quality of dedication to the ideal of a long-term study based upon love of and respect for the dignity of the individual within the group, and upon the satisfaction of making a single, valuable contribution to the increment of knowledge, without concern for credit, is fundamental and must exist in the research team. In this case, such qualities are found particularly in the local group who have been associated from the start. Without such personnel, intimately associated with the patients, without proper rapport between outside specialists and the patient community, and without mutual trust, understanding, and respect between local workers, outside specialists, and the central office, success cannot be assured, nor will continuity of observation be achieved.

Finally, it is essential to consider changes in medical practice and knowledge over the long period of such a study. A prospective study is of value only if the original diagnoses are sound—if the original medical work is well based. In this instance, diagnoses were based upon the best medical practice and knowledge available at the time. Review, 20 years later, of history, physical findings, and laboratory work of the original records reveals evidence of the high quality of medical skill which was exercised. When this is coupled with performance of newer laboratory procedures, there is added evidence of the firmness of original diagnosis. The syphilitic group, re-examined, is now confirmed to be predominantly syphilitic, and the control group to be free from evidence of syphilis.

The primary purpose of this study was, and continues to be, the determination of the outcome of untreated syphilis. However, in the accomplishment of this purpose, certain factors have been brought to light which merit discussion in relation to long-term disease studies in general.

One of the most important of these factors, and also one of the most difficult to control, is the consistency of techniques and standards used in the evaluation process. As an example, the STS, originally used for diagnostic purposes, was found during the course of the study to be of particular interest in relation to the occurrence of spontaneous cure and in the establishment of serologic trends for comparison with such factors in treated syphilis. Unfortunately, only a partial picture of the serologic pattern in this study group could be determined, due to the lack of consistency in the type of serologic test used and in the level of antigen sensitivity. Newer and more improved versions of the same test procedure may be added during the course of a study, but continuity of the original measurements by the original technique must be maintained along with these additions if meaningful results are to be obtained.

Another factor of particular importance is the preservation of all records and materials. For instance, the retention of pathologic specimens after the

it is probable that a few aortic murmurs might have been accentuated by having the patient sit up, lean forward, and exhale forcibly, as was done for auscultation. Having the patient exercise was useful, also, in auscultation, but impractical for our stethographic purpose.

Blood was drawn from syphilitic and nonsyphilitic individuals alike for VDRL slide and Kahn quantitative testing, as well as for the *Treponema pallidum* immobilization (TPI) test. All serologic tests for syphilis were performed at the Venereal Disease Research Laboratory at Chamblee, Georgia.

Spinal fluid examinations were done in 1951-1952 on only a few patients in whom it was felt to be definitely indicated by clinical findings. Omission of the test from the routine examination was made with great reluctance, since lumbar punctures had been done in 1932 on 271 of the original 408 syphilitic patients examined.¹ After twenty years, comparison of spinal fluid results with newer serologic techniques in the survivors would have been interesting. However, the emphasis in this survey upon epidemiologic tracing of every man made it impractical to employ a test which had been frightening to some superstitious patients, and, which might actually have driven them into hiding.⁹

DISCUSSION

It seems appropriate, after twenty years of experience, to comment upon some of the operational aspects of this study, which, to our knowledge, is the first prospective longitudinal long-term study involving the ideal of 100 per cent observation of a large group of diseased and control patients through life to autopsy.

Following these individuals through to autopsy is unique in a field study of this type, an autopsy rate of about 60 per cent of those who died is comparable to rates found in many teaching institutions. This phase of the study was made possible only because of the willingness of a private philanthropy, the Milbank Memorial Fund, to give moral commitment to such a lifetime study in order to make funds available for burial expenses and autopsy expenses. Without this suasion it would, we believe, have been impossible to secure the cooperation of the group and their families. Such private funds, committed for years in advance (and by an institution whose policies do not change with administrations or with single individuals, but which reflect decisions of technically competent boards of directors), would seem to be increasingly important for providing the type of support needed for the successful conclusion of similar studies in chronic disease.

A further factor to be considered is that of scientific interest on the part of the individuals concerned with working with the study. The one who sets up such a study may well assume that he, himself, may be dead by the time that the lifetime of many of the group is finished. The results of observation which will add to the sum of scientific knowledge may not begin to become available until years later; and at a time when the originator may be working in other fields and completely separated from the study. Those who contribute in the associated fields, in this case pathologic and serologic, add data which will be used years later by new investigators coming to the study; so that the early years,

original interpretation has been recorded makes it possible to review stained slides and to prepare new ones in accordance with improved techniques and methods of interpretation. Arrangements at the outset of a study for the preservation of all pathologic material will permit the review of an entire patient series at one time, applying identical techniques and criteria.

SUMMARY

1. This report, one of a series relating to the effect of untreated acquired syphilis in the male Negro, contains a history of the study and a description of the current status of the study population.

2. Included in the present study group are 408 syphilitic individuals and 192 nonsyphilitic controls who have maintained their status since the beginning of the study. Of the 408 in the syphilitic group, 51 per cent are living, 39 per cent are dead, and 10 per cent are of unknown status. In the nonsyphilitic group, 65 per cent are living, 26 per cent are dead, and 9 per cent are of unknown status.

3. On the basis of the individuals examined during the 1951-1952 survey, it is estimated that 70 per cent of the syphilitic group have remained untreated, 22.5 per cent have had inadequate treatment, and 7.5 per cent have been adequately treated. However, in terms of man-years, the study represents an aggregate of 5,494.5 man-years of untreated disease, 122 man-years of inadequately treated disease, and 28.5 man-years of adequately treated disease.

4. Physical examinations in this survey consisted of a review of the body systems, blood pressure determinations, funduscopic examinations, and neurologic examinations. Stethographic and electrocardiographic records were obtained on the patients.

5. Blood was drawn from syphilitic and nonsyphilitic patients for VDRL and Kahn quantitative testing, as well as for the TPI test.

6. This report has been prepared for the purpose of presenting information relating to the study group, which will serve as a basis for the discussion of the results of twenty years of clinical observation, to be presented in a subsequent report.⁷

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